Amendments to the Specification

Please replace the 3rd and 4th paragraphs on page 1 and 2 with the following amended paragraphs:

The cDNA of bone morphogenetic ~~,~~factor human MP52 was isolated for the first time in 1994 as an osteogenesis-related factor classified as a TGF-β superfamily (Biochem. Biophy. Res. Corom., Vol. 204, No.2, 1994). Then, an advanced genetic engineering technology has made it possible to prepare bone morphogenetic factor human MP52 without impairing its bone morphogenetic activity (WO96/33215). Bone morphogenetic factor human MP52 is stored under a lyophilized condition. It is, however, accompanied ~~wi th~~ with a drawback that a volume reduction (shrink) occurs during storage and cohesion of powders occurs at the time of reconstitution.

With a view to overcoming the above-described problems, amino acids, saccharides or polyhydric alcohols are used for BMP-2 which is a protein classified as the same TGF-β super-family and has properties closest to bone morphogenetic factor human MP52 (JP-A No. HEI 6-508777). The present inventors, therefore, attempted the application of such additives to bone morphogenetic factor human MP52 but could not overcome the above problems. Described specifically, cohesion at the time of reconstitution was observed even if a neutral or basic amino acid such as alanine, valine or lysine was added to bone morphogenetic factor human MP52 in an amount of 0.5 to 2.5% prior to

lyophilization. When a saccharide such as sucrose or dextran was added in an amount of 0.5 to 1%, ~~followeq~~ followed by lyophilization, color development to pale yellowish green and shrink were observed from the lyophilized product. ~~Wben~~ When a polyhydric alcohol such as sorbitol was added in an amount of 0.5 to 1%, followed by lyophilization, bone morphogenetic factor human MP52 was dissolved in the period of lyophilization, which made it impossible to prepare a lyophilized product.

Please replace the first two paragraphs on page 4 with the following amended paragraphs:

Furthermore it has surprisingly been found that the addition of anionic, non-ionic or zwitterionic detergents/substances to the described lyophilized composition clearly enhances the already highly positive effects of mannitol in terms of protein stability and avoiding aggregation at the redissolution. Another positive effect is that these detergents avoid ~~absorption~~ adsorption. Suitable detergents/substances are nonionic detergents/substances such as e.g. Brij (especially Brij-35, Brij-56, Brij-58), Digitonin, Hecameg, Nonidet P-40, n-nonyl-ß-glucopyranoside, n-octyl-glucopyranoside, polyoxyethylene derivatives (especially polyoxyethylene-polyoxypropylene ~~copolmers~~ copolymers), Triton (especially Triton X-100 and Triton X-114), Tween (especially Tween 20 and Tween 80), zwitterionic detergents such as e.g. CHAPS and CHAPSO, and anionic detergents such as DOC and SDS.

It is said that the preferred water content of a lyophilized product is generally 2%~~.~~ or lower. It was judged from the above findings that a bone morphogenetic factor human

MP52 composition containing mannitol in an amount of 5 to 50 mg, desirably 10 mg, per 1 mg of bone morphogenetic factor human MP52 is preferred as a pharmaceutical product.

Please replace Table 2 and the first part of the last paragraph on page 7 with the following amended paragraphs:

Table 2

composition	4°C	25°C
rhMP52 alone	ebf* was observed	ebf was observed
+ Mannitol,10 mg	ebf was observed	ebf was observed
+ Mannitol,25 mg	ebf was observed	ebf was observed
+ Mannitol,50 mg	ebf was observed	ebf was observed

*ebf: ectopic bone formation

Example 4 Improvement of the Mannitol-containing composition by addition of a detergent

The aqueous mannitol-containing solution of example 1 was further supplemented with different types of detergents/substances (Brij-35, Brij-56, Brij-58, Digitonin, Hecameg, Nonidet P-40, n-nonyl-ß-glucopyranoside, n-octyl-glucopyranoside, polyoxyethylene-poloxypropylene copolymers, Triton X-100, Triton X-114, Tween 20, Tween 80, CHAPS, CHAPSO,